REMARKS

It is respectfully requested that this application be reconsidered in view of the above amendments and the following remarks and that all of the claims remaining be allowed.

Request for Continued Examination

Applicants hereby request continued examination of the present application under 37 C.F.R. §1.114.

Claim Amendments

Claim 21 has been amended by reversing step (a) and step (b). Claim 21 has further been amended by adding the recitation "such that the amino acids from the epitope in the b_i, c_i, e_i, f_i and g_i positions are interrupted by the amino acids in the a and d positions". Support for these amendments can be found, for example, at page 9, lines 24-29.

Similarly, claim 30 has been amended to recite "and the sequence $(b_i c_i e_i f_i g_i)_n$ is interrupted by amino acids a and d in $(ab_i c_i de_i f_i g_i)_n$", for which support can be found, for example, at page 9, lines 24-29.

No new matter has been added by these amendments. The Examiner is hereby requested to enter these amendments.

Applicants submit that all claim amendments presented herein or previously are made solely in the interest of expediting allowance of the claims and should not be interpreted as acquiescence to any rejections or ground of unpatentability. Applicants reserve the right to file at least one continuing application to pursue any subject matter that is canceled or removed from prosecution due to the amendments.

Rejection under 35 U.S.C. §102:

The rejection of claims 21-25 and 30-34 under 35 U.S.C. §102(e) over Cooper et al. (U.S. Patent No. 6,174,528, hereinafter "the Cooper patent") is respectfully traversed for the reasons set forth below.

The standard of anticipation under 35 U.S.C. §102 is that each and every element of the claim must be found in the cited reference. *In re Marshall* (CCPA 1978), 198 USPQ 344.

The Cooper patent does not teach each and every element of the claimed invention. Claim 21 of the present application is directed to a coiled-coil polypeptide comprising the formula $(ab_i c_i de_i f_i g_i)_n$, where $i=1,2,....,n$, and n is at least three, said polypeptide being prepared by

(a)   selecting a solvent-accessible region of an epitope of a selected natural protein, wherein said region is not in a coiled-coil conformation in its native state, and inserting the amino acids from said region into the b_i, c_i, e_i, f_i and g_i positions; and

(b)   independently inserting an amino acid selected from the group consisting of leucine, isoleucine, valine, phenylalanine, methionine, tyrosine, and derivatives thereof, into each of the a and d positions such that the amino acids from the epitope in the b_i, c_i, e_i, f_i and g_i positions are interrupted by the amino acids in the a and d positions;

wherein $(ab_i c_i de_i f_i g_i)_n$, forms a coiled-coil.

Thus, the polypeptide of claim 21 is prepared by inserting amino acids from a pre-selected group into the <u>a and d</u> positions of the formula $(ab_i c_i de_i f_i g_i)_n$ and a solvent-accessible region into the <u>b_i</u>, <u>c_i</u>, <u>e_i</u>, <u>f_i and g_i</u> positions. The solvent-accessible region is from an epitope of a natural protein, wherein the region is <u>not in a coiled-coil conformation in its native state</u>. Claims 22-25 depend from claim 21, thereby reciting all the elements of claim 21.

The Cooper patent teaches that one sequence can be embedded within a second sequence (see, for example, column 2, lines 19-21). Indeed, all examples in the Cooper patents teach the

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embedding of a short peptide sequence in the middle of a second sequence, resulting in a fusion protein. For instance, in Example 12 of the Cooper patent, a series of 12-mer peptides overlapping by 1 residue was derived from the streptococcal M protein peptide p145, and each 12-mer was embedded into a GCN4 sequence. Thus, the resulting chimeric peptides have a 12 amino acid sequence from p145 flanked by GCN4 sequences. The polypeptides of the claimed invention, on the other hand, contain amino acid residues from a first sequence in the b_i, c_i, e_i, f_i and g_i positions, which are interrupted by amino acids from the a and d positions.

The Advisory Action states that the claimed invention does not expressly recite that the sequence of the b_i, c_i, e_i, f_i and g_i positions is interrupted by amino acids from the a and d positions. As amended, the claims now expressly recite "such that the amino acids from the epitope in the b_i, c_i, e_i, f_i and g_i positions are interrupted by the amino acids in the a and d positions". Thus, the Cooper patent does not teach each and every element of the claimed invention.

Furthermore, the Cooper patent does not teach a coiled-coil polypeptide that comprises a region which is not in a coiled-coil conformation in its native state. Instead, the Cooper patent teaches:

> In accordance with the present invention, overlapping peptides derived from a conformational epitope are embedded within a peptide having a similar native conformation. (column 2, lines 19-21; emphasis added)

> Accordingly, one aspect of the present invention contemplates a chimeric peptide comprising a first amino acid sequence comprising a conformational epitope inserted within a second amino acid sequence wherein said first and second amino acid sequences are derived from peptides, polypeptides or proteins having similar native conformations. (column 2, lines 26-32; emphasis added)

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The Cooper patent further teaches that the second amino acid sequence constitutes a "framework peptide" and provides an appropriate conformation for the chimeric peptide (column 2, lines 33-36). In particular, the conformation may be coiled-coil:

> In its most preferred embodiment, the framework peptide assumes a α-helical coiled coil conformation and is, therefore, useful in presenting epitopes present in the first amino acid sequence in a similar conformation, i.e. an α-helical coiled coil conformation. (column 2, lines 39-43)

Accordingly, a coiled-coil peptide taught by the Cooper patent would contain a first amino acid sequence embedded in a second amino acid sequence, and both sequences are in an α-helical coiled coil conformation in their native state. In contrast, claims 21-25 of the present application require the b_i, c_i, e_i, f_i and g_i positions of the coiled-coil to be occupied by a solvent-accessible region of an epitope of a selected natural protein, wherein said region is not in a coiled-coil conformation in its native state. Nowhere does the Cooper patent teach the insertion of sequences from a non-coiled-coil protein into a coiled-coil framework to prepare a coiled-coil polypeptide.

The Advisory Action states that the Cooper patent teaches the insertion of a conformational B-cell epitope from Streptococcal M protein, which "inherently does not have the structural configuration to form a coiled-coil". This assertion is unfound because the Streptococcal M protein does form a coiled coil, and the Cooper patent teaches the insertion of a coiled coil Streptococcal M protein epitope into a coiled coil template. Applicants wish to point to lines 25-28 in column 1 of the Cooper patent:

> More than 200 proteins have now been predicted to contain coiled coil domains (Lupas et al., 1991). These include surface proteins of certain bacteria such as streptococcal protein A and M proteins

Clearly, the streptococcal M protein can form a coiled coil, contrary to the Advisory Action's contention.

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Applicants also wish to point to claim 3 of the Cooper patent, which reads:

3.   A chimeric peptide according to claim 1 or 2, wherein said first amino acid sequence is derived from the streptococcal M protein.

The base claims 1 and 2 are reproduced below:

1.   A chimeric peptide comprising:

(i) a first amino acid sequence which, in its native state, presents a conformational epitope, said conformational epitope not being present in the first amino acid sequence in an isolated state; and

(ii) a second amino acid sequence which has a conformation similar to the native conformation of the first amino acid sequence;

wherein the first amino acid sequence is inserted within the second amino acid sequence such that the first amino acid sequence presents the conformational epitope.

2.   A chimeric peptide according to claim 1, wherein said second amino acid sequence assumes a alpha-helical coiled coil conformation.

In these claims, the first sequence, in its native state, has similar conformation with the second sequences, which is a coiled coil conformation in claim 2. Since the streptococcal M protein is the first sequence in claim 3 and claim 3 depends from claim 2, the streptococcal M protein sequence to be inserted must be a coiled coil in its native state. Therefore, the assertion of the Advisory Action that the Streptococcal M protein is a non-coiled coil protein is not supported, and the Cooper patent does not teach each and every element of the present invention.

Similarly, claim 30 of the present application is directed to a coiled-coil polypeptide, comprising an amino acid sequence represented by $(ab_ic_ide_if_ig_i)_n$, where

$i=1,2,....,n$, and n is at least three;

a and d are amino acids each independently selected from the group consisting of leucine, isoleucine, valine, phenylalanine, methionine, tyrosine, and derivatives thereof;

$(b_ic_ie_if_ig_i)_n$ is a sequence of amino acids from a solvent-accessible region of an epitope from a selected natural protein, wherein said region is not in a coiled-coil conformation

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in its native state, and the sequence $(b_i c_i e_i f_i g_i)_n$ is interrupted by amino acids a and d in $(ab_i c_i de_i f_i g_i)_n$;; and

wherein $(ab_i c_i de_i f_i g_i)_n$ forms a coiled coil.

Claims 31-34 depend from claim 30, thus reciting all the elements of claim 30. Again, the Cooper patent does not teach the polypeptides of claims 31-34, *e.g.*, with respect to the region of the polypeptides that is derived from a non-coiled-coil region.

Therefore, the Cooper patent does not teach each and every element of the claimed invention. Since the requirement under 35 U.S.C. §102 is not met, Applicants respectfully request that this rejection be withdrawn.

Conclusions

For the reasons set forth above, Applicants submit that the claims of this application are patentable. Reconsideration and withdrawal of the Examiner's rejections are hereby requested. Allowance of the claims remaining in this application is earnestly solicited.

In the event that a telephone conversation could expedite the prosecution of this application, the Examiner is requested to call the undersigned at (650) 839-5044.
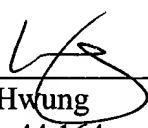
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Enclosed is a $385.00 check for the RCE fee required under 37 CFR 1.17(e) and a

$210.00 check for the Petition for Extension of Time fee. Please apply any other charges or

credits to deposit account 06-1050.

Respectfully submitted,

Date: Feb. 17, 2004

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